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NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 7	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 8	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 9	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 10	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 11	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 12	OCT 19	E-mail format enhanced
NEWS 13	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 14	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 15	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 16	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 17	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 18	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 19	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 20	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 21	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 22	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 23	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 24	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 25	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 26	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 27	DEC 18	CA/CAplus patent kind codes updated
NEWS 28	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 29	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 30	DEC 27	CA/CAplus enhanced with more pre-1907 records

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),

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AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 15:11:47 ON 31 DEC 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:11:59 ON 31 DEC 2006
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STRUCTURE FILE UPDATES: 29 DEC 2006 HIGHEST RN 916574-44-2
DICTIONARY FILE UPDATES: 29 DEC 2006 HIGHEST RN 916574-44-2

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http://www.cas.org/ONLINE/UG/regprops.html

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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1 STR

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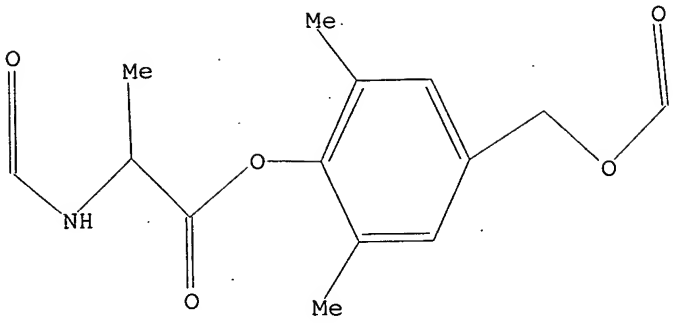

Structure attributes must be viewed using STN Express query preparation.

=> s L1 full
FULL SEARCH INITIATED 15:12:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 533 TO ITERATE

100.0% PROCESSED 533 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L2 8 SEA SSS FUL L1

=> fil hcap
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

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FILE COVERS 1907 - 31 Dec 2006 VOL 146 ISS 2
FILE LAST UPDATED: 29 Dec 2006 (20061229/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> l2
L3 6 L2

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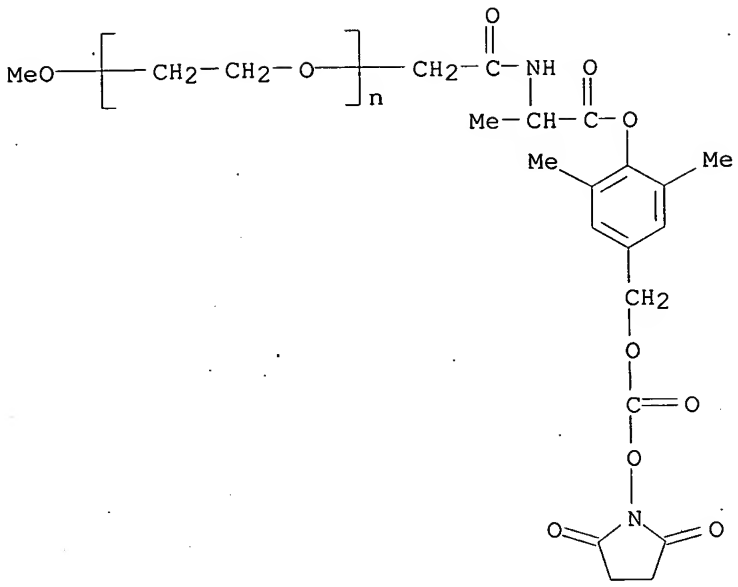
=> d l3 1-6 ibib abs hitstr

L3 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:562019 HCAPLUS
DOCUMENT NUMBER: 143:253714
TITLE: A New platform for oligonucleotide delivery utilizing the PEG prodrug approach
AUTHOR(S): Zhao, Hong; Greenwald, Richard B.; Reddy, Prasanna; Xia, Jing; Peng, Ping
CORPORATE SOURCE: Enzon Pharmaceuticals Inc., Piscataway, NJ, 08854, USA
SOURCE: Bioconjugate Chemistry (2005), 16(4), 758-766
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The oligonucleotide (oligo, ODN), Genasense (GS), an ODN currently waiting for FDA approval, was chosen as a model and modified with a 5' or 3' aminohexyl functionality (1 and 4, resp.) using solid-state synthesis. These amino derivs. were reacted with different releasable PEGs (rPEGs). The in vitro results of the PEG-modified oligos (Table 1) clearly showed a substantial increase in rat plasma half-life and enhanced stability against a variety of nucleases, especially the predominant nuclease (PEII) in mammals, which is the main source of oligo degradation in cells. The advantage of using a PEG prodrug approach was further demonstrated by the pharmacokinetic (PK) results, which exhibited much greater Cmax, plasma half-life, and area under the curve (AUC) for 3 compared to unmodified GS. A key step in the synthesis of ODN prodrug conjugates with a dye label was also accomplished successfully by employing dihydropyran derivs. of alcs. and acids as orthogonal protecting groups during the synthesis.

IT 780810-34-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(new platform for oligonucleotide delivery utilizing PEG prodrug approach)

RN 780810-34-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902399 HCAPLUS
DOCUMENT NUMBER: 141:395768
TITLE: Preparation of polyethylene glycol oligodeoxyribonucleotide conjugates as antitumor prodrugs
INVENTOR(S): Zhao, Hong; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092191	A2	20041028	WO 2004-US10852	20040409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004230927	A1	20041028	AU 2004-230927	20040409
CA 2520550	A1	20041028	CA 2004-2520550	20040409
US 2004235773	A1	20041125	US 2004-822205	20040409

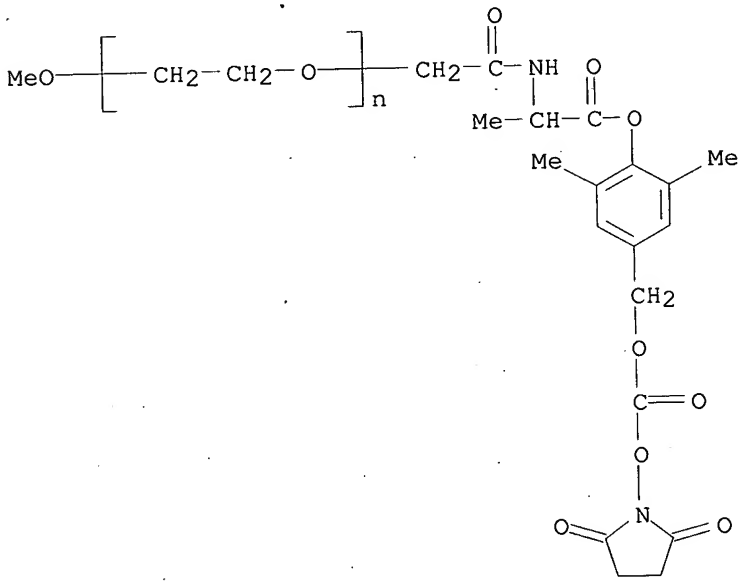
T.S. Heard Ph.D.

EP 1620450 A2 20060201 EP 2004-749888 20040409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
FI 2005001017 A 20051010 FI 2005-1017 20051010
PRIORITY APPLN. INFO.: US 2003-462070P P 20030413
WO 2004-US10852 W 20040409

AB Polyethylene glycol oligodeoxyribonucleotide conjugates were prepared as as antitumor prodrugs. Confirmation of in vitro activity and in mice of antisense PEG conjugates bcl-2 protein has been shown to have significant anti-apoptotic activity in prostate cancer cells. Down regulation of bcl-2 protein in prostate cancer cells is confirmed by cell death, and induction of cell death by bcl-2 antisense PEG conjugates was employed to confirm the successful intracellular delivery of the antisense oligonucleotides. Pharmacokinetic studies for title compds. were reported.

IT 780810-34-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polyethylene glycol oligodeoxyribonucleotide conjugates as antitumor prodrugs)

RN 780810-34-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



L3 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:430983 HCAPLUS
DOCUMENT NUMBER: 141:12275
TITLE: Preparation of polymeric prodrugs of vancomycin
INVENTOR(S): Zhao, Hong; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

T.S. Heard Ph.D.

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004044222	A2	20040527	WO 2003-US35740		20031111
WO 2004044222	A3	20041021			
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003287605	A1	20040603	AU 2003-287605		20031111
US 2004136947	A1	20040715	US 2003-705743		20031111
PRIORITY APPLN. INFO.:			US 2002-425892P	P	20021112
			WO 2003-US35740	W	20031111

OTHER SOURCE(S): MARPAT 141:12275

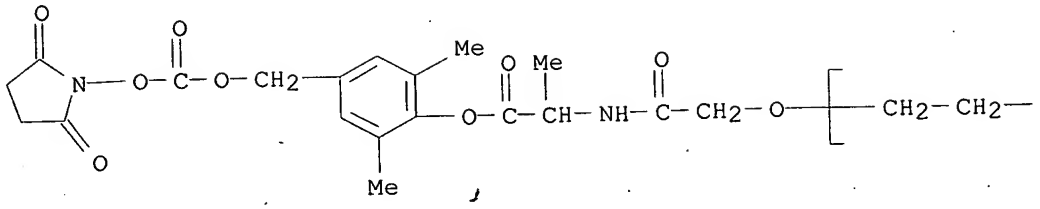
AB Methods of preparing vancomycin-polymer conjugates are disclosed. In preferred aspects, polymer residues which are preferably releasable, are selectively attached to the sugar amino and/or N-Me amino groups of vancomycin and related compds. Vancomycin-polymer (e.g., PEG derivs.) conjugates made by the methods and methods of treatment using the conjugates are also disclosed. Some of the compds. had significant antibacterial activity.

IT 693811-22-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymeric prodrugs of vancomycin)
RN 693811-22-2 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, N3'',N3''''-diether with N3''-[[[4-[(2S)-2-[(hydroxyacetyl)amino]-1-oxopropoxy]-3,5-dimethylphenyl]methoxy]carbonyl]vancomycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 693811-21-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polymeric prodrugs of vancomycin)
RN 693811-21-1 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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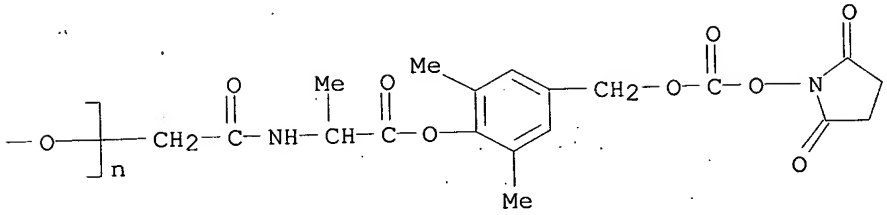


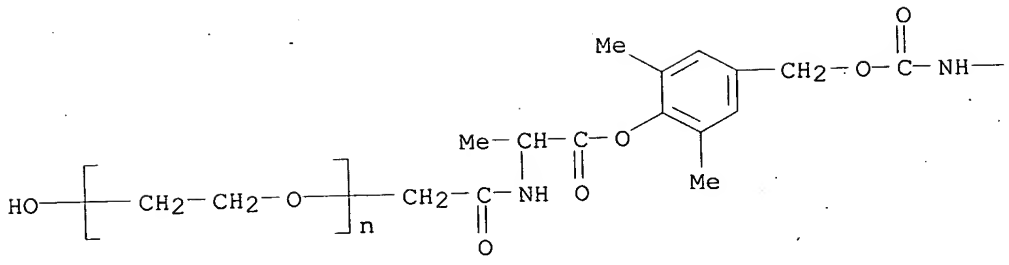
L3 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:784805 HCAPLUS
DOCUMENT NUMBER: 140:19693
TITLE: Poly(ethylene glycol) transport forms of vancomycin: a long-lived continuous release delivery system
AUTHOR(S): Greenwald, Richard B.; Zhao, Hong; Xia, Jing; Martinez, Anthony
CORPORATE SOURCE: Enzon Pharmaceuticals Inc., Piscataway, NJ, 00854, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(23), 5021-5030
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The facile reaction of vancomycin with various PEG linkers, at the V3 position, has been selectively accomplished by using an excess of base in DMF. Using rPEG as a blocking group for V3 provides crystalline derivs. that can be further PEGylated to give pure V3-X1 latentiated species (transport forms). V3 tetrameric species were also prepared in order to increase the loading of drug on PEG. All PEG-vancomycin transport forms show significant antibacterial activity that is on the same order of native vancomycin. Significant increases in the AUC were observed for all PEG-vancomycin conjugates thus making them potential single dose therapies.

IT 627539-78-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(poly(ethylene glycol) transport forms of vancomycin offering a long-lived continuous release delivery system)

RN 627539-78-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, N3''-ether with N3''-[[[4-[(2S)-2-[(hydroxyacetyl)amino]-1-oxopropoxy]-3,5-dimethylphenyl]methoxy]carbonyl]vancomycin (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



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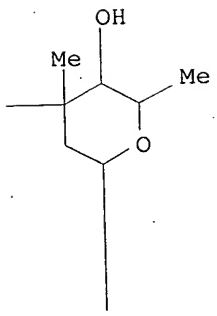

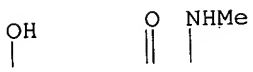

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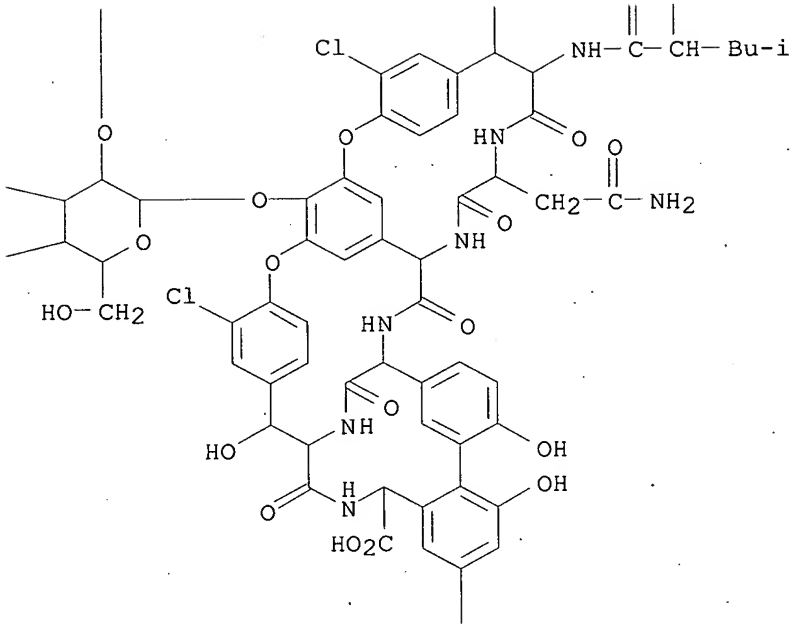
PAGE 2-A

PAGE 2-B



PAGE 3-B

IT 627539-76-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(poly(ethylene glycol) transport forms of vancomycin offering a long-lived continuous release delivery system)

RN 627539-76-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-hydroxy- (9CI) (CA INDEX NAME)

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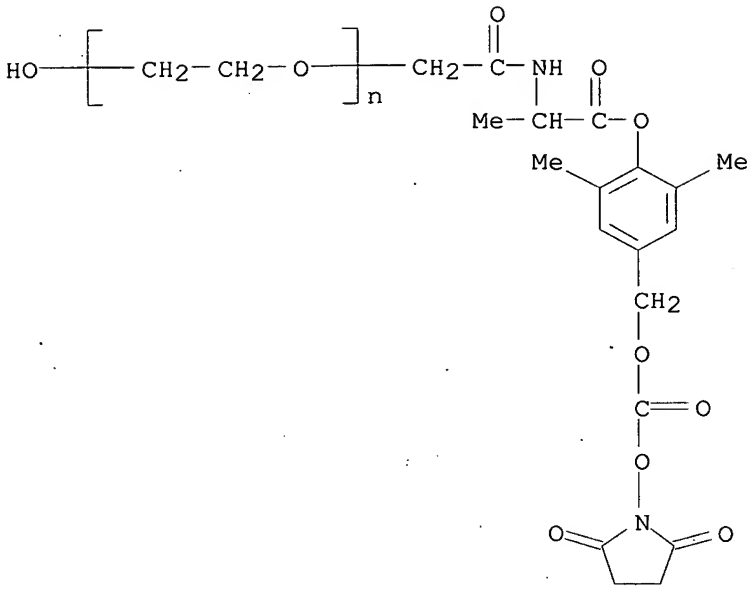

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:657915 HCAPLUS
DOCUMENT NUMBER: 137:206534
TITLE: Terminally-branched polymeric linkers and polymeric conjugates as prodrugs
INVENTOR(S): Choe, Yun Hwang; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002065988	A2	20020829	WO 2002-US4781	20020219
WO 2002065988	A3	20030410		
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CA 2437989	A1	20020829	CA 2002-2437989	20020219
US 2002183259	A1	20021205	US 2002-78730	20020219
EP 1362053	A2	20031119	EP 2002-721033	20020219

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JP 2004532289 T 20041021 JP 2002-565549 20020219
PRIORITY APPLN. INFO.: US 2001-270009P P 20010220
WO 2002-US4781 W 20020219

OTHER SOURCE(S): MARPAT 137:206534

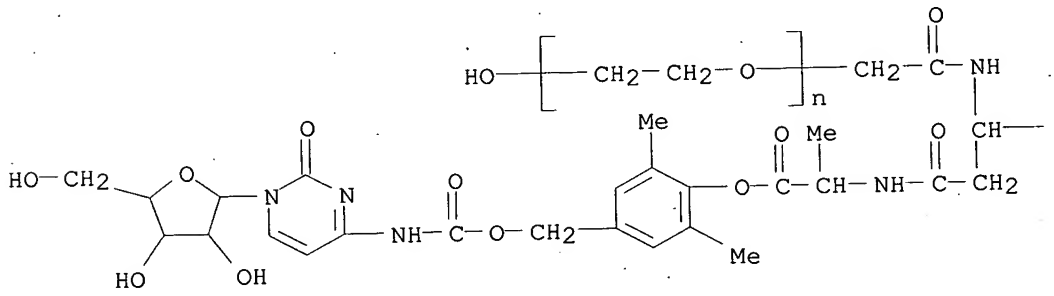
AB Terminally-branched polymeric prodrug platforms capable of high degrees of loading are disclosed. In preferred aspects of the invention, the prodrug platform releases multiple parent compds. after each branch holding the active agent undergoes a benzyl elimination reaction. Methods of preparing the prodrugs and using the same in the treatment of mammals are also disclosed. For example, a polyethylene glycol-cytosine arabinoside (PEG-Ara-C) conjugate was prepared The PEG-Ara-C conjugate demonstrated in tumor-bearing mice about equivalent antitumor activity with native Ara-C at only 20% of the active parent compound's dose. The IC50 for the PEG-Ara-C conjugate and the native Ara-C was 448 and 10 nM, resp., as determined in vitro using the P388/O (murine lymphoid neoplasm) cell line.

IT 452369-80-1P
RL: AMX (Analytical matrix); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)

RN 452369-80-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 1-monoether with N-(hydroxyacetyl)-L-aspartoylbis[L-alanine] bis[4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



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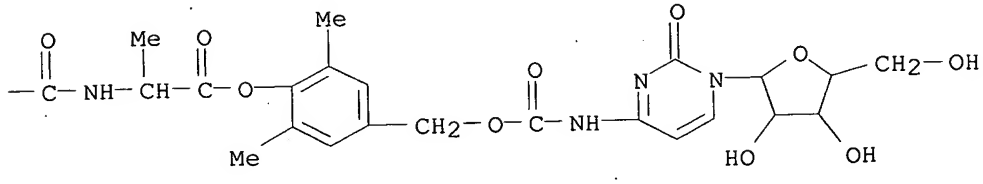
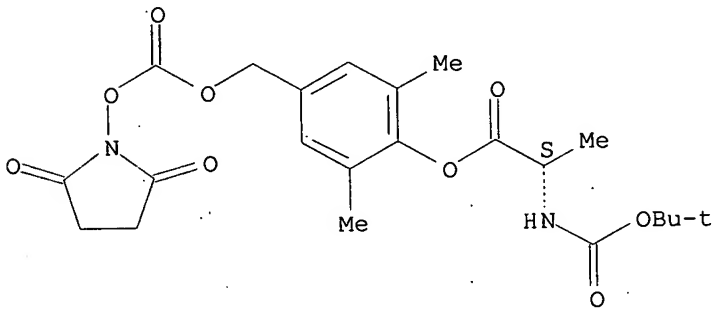


IT 452369-76-5P 452369-77-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)

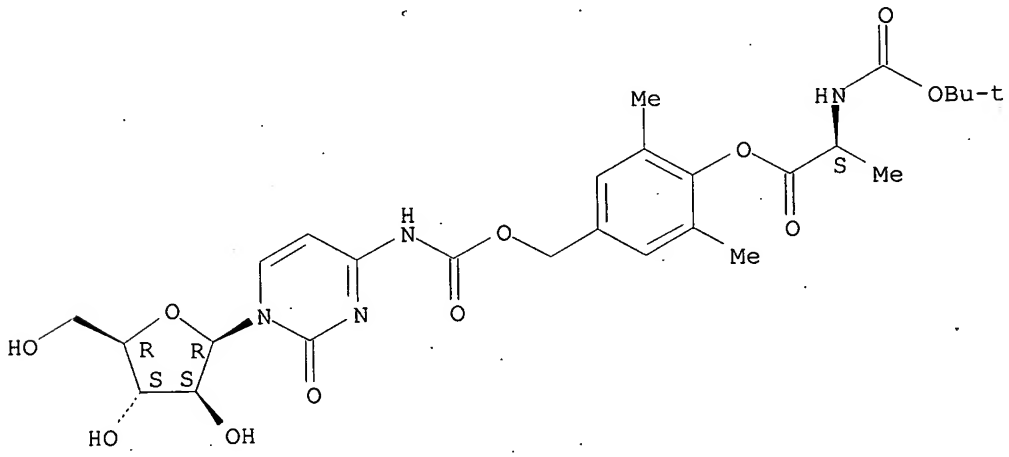
RN 452369-76-5 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 452369-77-6 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:130614 HCAPLUS
DOCUMENT NUMBER: 137:341957
TITLE: Anticancer drug delivery systems: multi-loaded N4-acyl poly(ethylene glycol) prodrugs of ara-C. II. Efficacy in ascites and solid tumors
AUTHOR(S): Choe, Yun H.; Conover, Charles D.; Wu, Dechun; Royzen, Maksim; Gervacio, Yoany; Borowski, Virna; Mehlig,

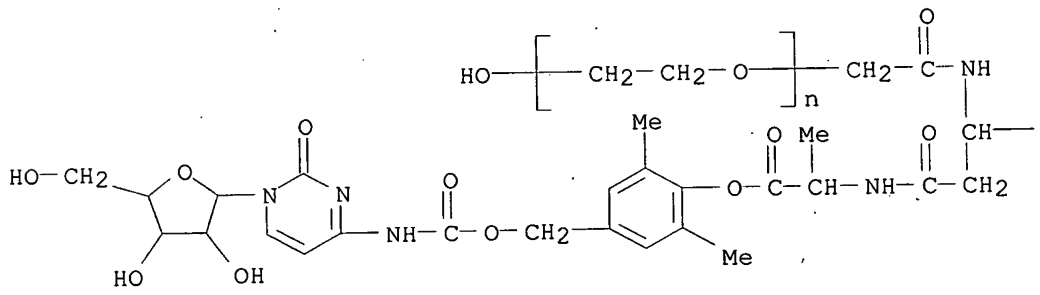
Mary; Greenwald, Richard B.
CORPORATE SOURCE: Enzon, Inc., Piscataway, NJ, 08854-3969, USA
SOURCE: Journal of Controlled Release (2002), 79(1-3), 55-70
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of branched PEG (40,000) acids has been achieved using aspartic acid (Asp) and AspAsp dendrons. Complete conjugation of these dendritic acids with cytosine arabinoside (ara-C) was achieved by the use of spacers that allowed a greater separation of the branches to accommodate several large ara-C mols. in proximity to each other. The tetrameric and octameric PEG-ara-C amide prodrugs were much more effective in the treatment of solid and ascites tumors compared to the native drug. The greater loading of the PEG backbone appears to have achieved a min. threshold concentration for the therapeutic delivery of ara-C.

IT 452369-80-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and efficacy in ascites and solid tumors of multi-loaded N4-acyl polyethylene glycol prodrugs of ara-C)

RN 452369-80-1 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 1-monoether with N-(hydroxyacetyl)-L-aspartoylbis[L-alanine] bis[4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



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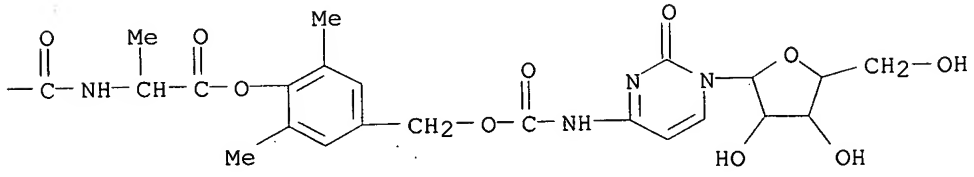


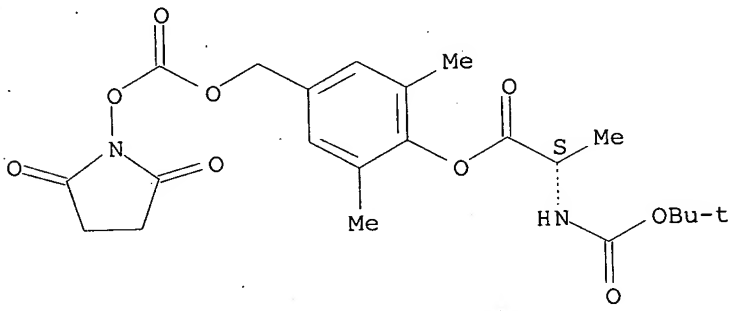
IT 452369-76-5P 452369-77-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and efficacy in ascites and solid tumors of multi-loaded N4-acyl polyethylene glycol prodrugs of ara-C)

RN 452369-76-5 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

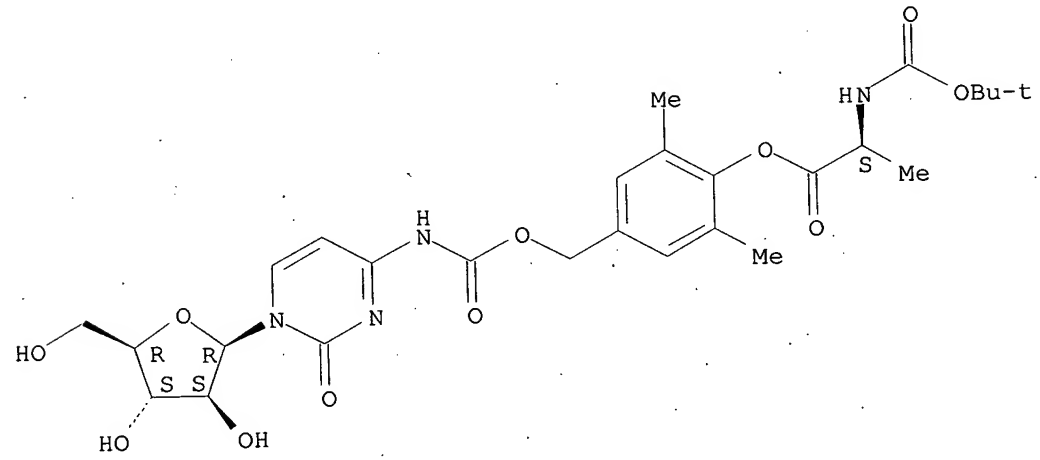
Absolute stereochemistry.



RN 452369-77-6 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L1 STR

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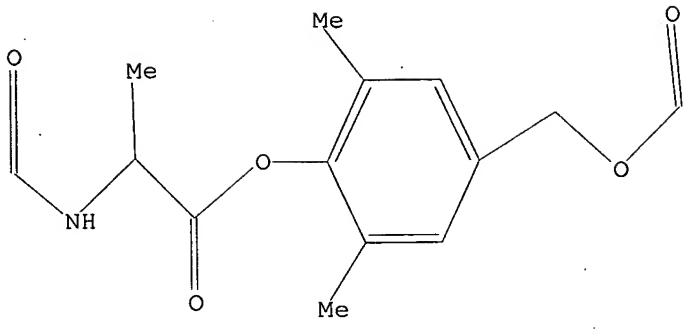

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L3 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L2

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FILE 'REGISTRY' ENTERED AT 15:11:59 ON 31 DEC 2006
L1 STRUCTURE UPLOADED
DIS
L2 8 SEA SSS FUL L1

FILE 'HCAPLUS' ENTERED AT 15:12:26 ON 31 DEC 2006
L3 6 SEA ABB=ON PLU=ON L2
D L3 1-6 IBIB ABS HITSTR
D QUE STAT

FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 DEC 2006 HIGHEST RN 916574-44-2
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FILE HCAPLUS

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FILE COVERS 1907 - 31 Dec 2006 VOL 146 ISS 2
FILE LAST UPDATED: 29 Dec 2006 (20061229/ED)

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'HID' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
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IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

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SIBIB ------- IBIB, no citations

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containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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APPS -------- AI, PRAI
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CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers; SCAN must be entered on the same line as the DISPLAY, e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

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SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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codes.  For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
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                                                 ENTRY    SESSION
FULL ESTIMATED COST                              61.02     228.17

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                              -4.50      -4.50

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     FILE 'REGISTRY' ENTERED AT 15:11:59 ON 31 DEC 2006
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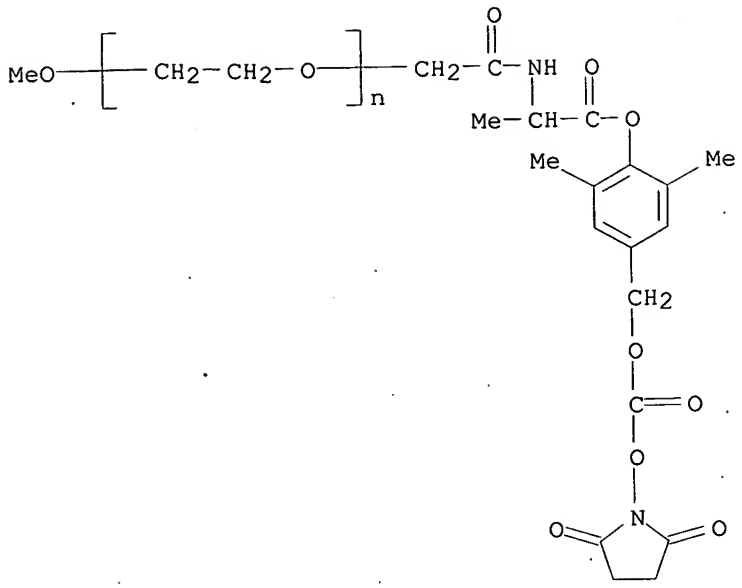
L4 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:562019 HCAPLUS
DOCUMENT NUMBER: 143:253714
TITLE: A New platform for oligonucleotide delivery utilizing the PEG prodrug approach
AUTHOR(S): Zhao, Hong; Greenwald, Richard B.; Reddy, Prasanna; Xia, Jing; Peng, Ping
CORPORATE SOURCE: Enzon Pharmaceuticals Inc., Piscataway, NJ, 08854, USA
SOURCE: Bioconjugate Chemistry (2005), 16(4), 758-766
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The oligonucleotide (oligo, ODN), Genasense (GS), an ODN currently waiting for FDA approval, was chosen as a model and modified with a 5' or 3' aminohexyl functionality (1 and 4, resp.) using solid-state synthesis. These amino derivs. were reacted with different releasable PEGs (rPEGs). The in vitro results of the PEG-modified oligos (Table 1) clearly showed a substantial increase in rat plasma half-life and enhanced stability against a variety of nucleases, especially the predominant nuclease (PEII) in mammals, which is the main source of oligo degradation in cells. The advantage of using a PEG prodrug approach was further demonstrated by the pharmacokinetic (PK) results, which exhibited much greater Cmax, plasma half-life, and area under the curve (AUC) for 3 compared to unmodified GS. A key step in the synthesis of ODN prodrug conjugates with a dye label was also accomplished successfully by employing dihydropyran derivs. of alcs. and acids as orthogonal protecting groups during the synthesis.
IT 780810-34-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(new platform for oligonucleotide delivery utilizing PEG prodrug approach)
RN 780810-34-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902399 HCAPLUS
DOCUMENT NUMBER: 141:395768
TITLE: Preparation of polyethylene glycol oligodeoxyribonucleotide conjugates as antitumor prodrugs
INVENTOR(S): Zhao, Hong; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092191	A2	20041028	WO 2004-US10852	20040409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2520550	A1	20041028	CA 2004-2520550	20040409
US 2004235773	A1	20041125	US 2004-822205	20040409

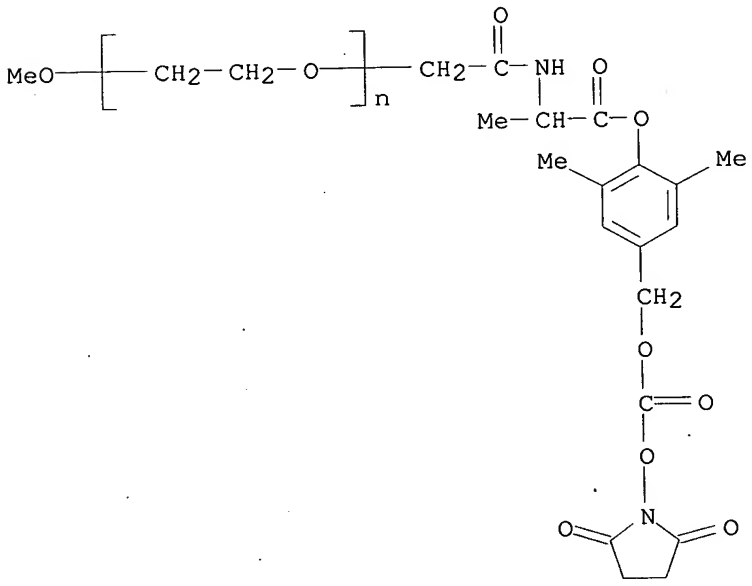
T.S. Heard Ph.D.

EP 1620450 A2 20060201 EP 2004-749888 20040409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
FI 2005001017 A 20051010 FI 2005-1017 20051010
PRIORITY APPLN. INFO.: US 2003-462070P P 20030413
WO 2004-US10852 W 20040409

AB Polyethylene glycol oligodeoxyribonucleotide conjugates were prepared as as antitumor prodrugs. Confirmation of in vitro activity and in mice of antisense PEG conjugates bcl-2 protein has been shown to have significant anti-apoptotic activity in prostate cancer cells. Down regulation of bcl-2 protein in prostate cancer cells is confirmed by cell death, and induction of cell death by bcl-2 antisense PEG conjugates was employed to confirm the successful intracellular delivery of the antisense oligonucleotides. Pharmacokinetic studies for title compds. were reported.

IT 780810-34-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polyethylene glycol oligodeoxyribonucleotide conjugates as antitumor prodrugs)

RN 780810-34-6 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:430983 HCAPLUS
DOCUMENT NUMBER: 141:12275
TITLE: Preparation of polymeric prodrugs of vancomycin
INVENTOR(S): Zhao, Hong; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

T.S. Heard Ph.D.

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004044222	A2	20040527	WO 2003-US35740	20031111
WO 2004044222	A3	20041021		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2004136947	A1	20040715	US 2003-705743	20031111
PRIORITY APPLN. INFO.:			US 2002-425892P P	20021112
			WO 2003-US35740 W	20031111

OTHER SOURCE(S): MARPAT 141:12275

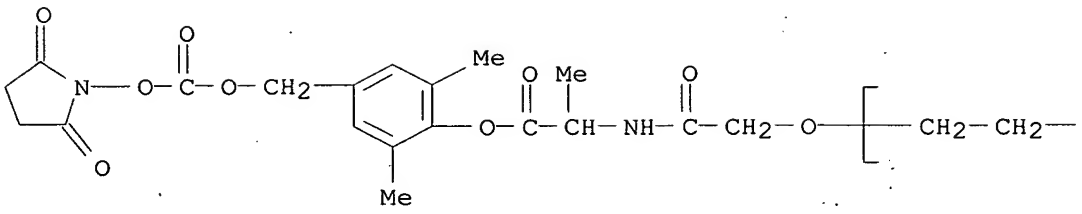
AB Methods of preparing vancomycin-polymer conjugates are disclosed. In preferred aspects, polymer residues which are preferably releasable, are selectively attached to the sugar amino and/or N-Me amino groups of vancomycin and related compds. Vancomycin-polymer (e.g., PEG derivs.) conjugates made by the methods and methods of treatment using the conjugates are also disclosed. Some of the compds. had significant antibacterial activity.

IT 693811-22-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymeric prodrugs of vancomycin)
RN 693811-22-2 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, N3'',N3''''-diether with N3''-[[[4-[(2S)-2-[(hydroxyacetyl)amino]-1-oxopropoxy]-3,5-dimethylphenyl]methoxy]carbonyl]vancomycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 693811-21-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polymeric prodrugs of vancomycin)
RN 693811-21-1 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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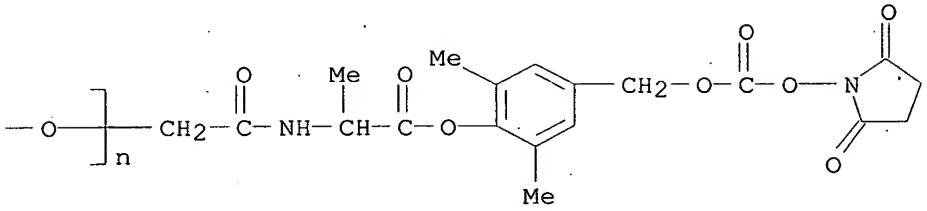


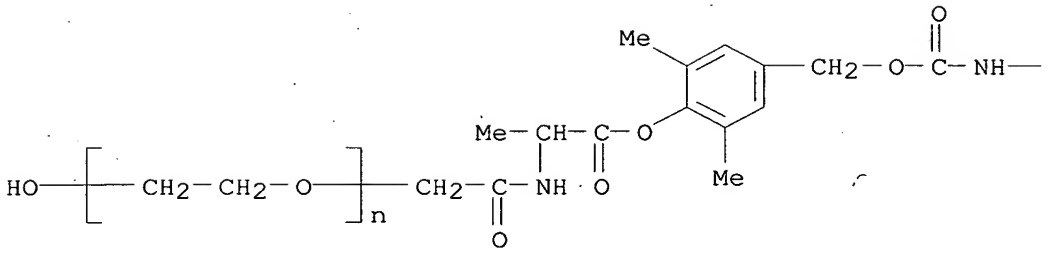
L4 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:784805 HCAPLUS
DOCUMENT NUMBER: 140:19693
TITLE: Poly(ethylene glycol) transport forms of vancomycin: a long-lived continuous release delivery system
AUTHOR(S): Greenwald, Richard B.; Zhao, Hong; Xia, Jing; Martinez, Anthony
CORPORATE SOURCE: Enzon Pharmaceuticals Inc., Piscataway, NJ, 00854, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(23), 5021-5030
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The facile reaction of vancomycin with various PEG linkers, at the V3 position, has been selectively accomplished by using an excess of base in DMF. Using rPEG as a blocking group for V3 provides crystalline derivs. that can be further PEGylated to give pure V3-X1 latentiated species (transport forms). V3 tetrameric species were also prepared in order to increase the loading of drug on PEG. All PEG-vancomycin transport forms show significant antibacterial activity that is on the same order of native vancomycin. Significant increases in the AUC were observed for all PEG-vancomycin conjugates thus making them potential single dose therapies.

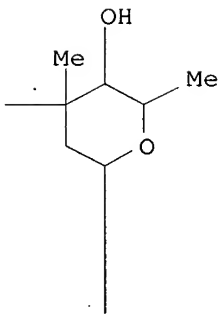
IT 627539-78-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(poly(ethylene glycol) transport forms of vancomycin offering a long-lived continuous release delivery system)

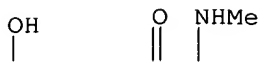
RN 627539-78-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, N3''-ether with N3''-[[[4-[(2S)-2-[(hydroxyacetyl)amino]-1-oxopropoxy]-3,5-dimethylphenyl]methoxy]carbonyl]vancomycin (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



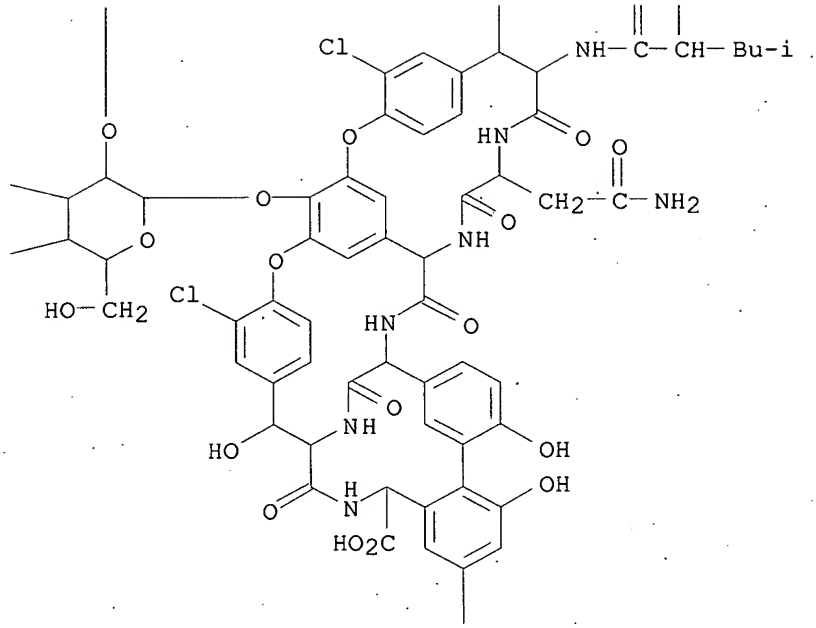
PAGE 1-B





PAGE 2-A

PAGE 2-B



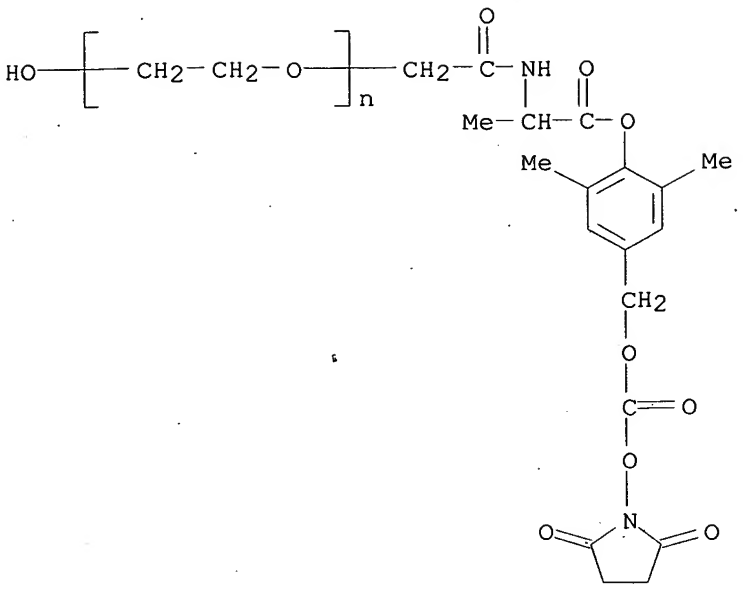
PAGE 3-B

IT 627539-76-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(poly(ethylene glycol) transport forms of vancomycin offering a long-lived continuous release delivery system)

RN 627539-76-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-hydroxy- (9CI) (CA INDEX NAME)

T.S. Heard Ph.D.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:657915 HCAPLUS
DOCUMENT NUMBER: 137:206534
TITLE: Terminally-branched polymeric linkers and polymeric conjugates as prodrugs
INVENTOR(S): Choe, Yun Hwang; Greenwald, Richard B.
PATENT ASSIGNEE(S): Enzon, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002065988	A2	20020829	WO 2002-US4781	20020219
WO 2002065988	A3	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2437989	A1	20020829	CA 2002-2437989	20020219
US 2002183259	A1	20021205	US 2002-78730	20020219
EP 1362053	A2	20031119	EP 2002-721033	20020219

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004532289 T 20041021 JP 2002-565549 20020219
PRIORITY APPLN. INFO.: US 2001-270009P P 20010220
WO 2002-US4781 W 20020219

OTHER SOURCE(S): MARPAT 137:206534

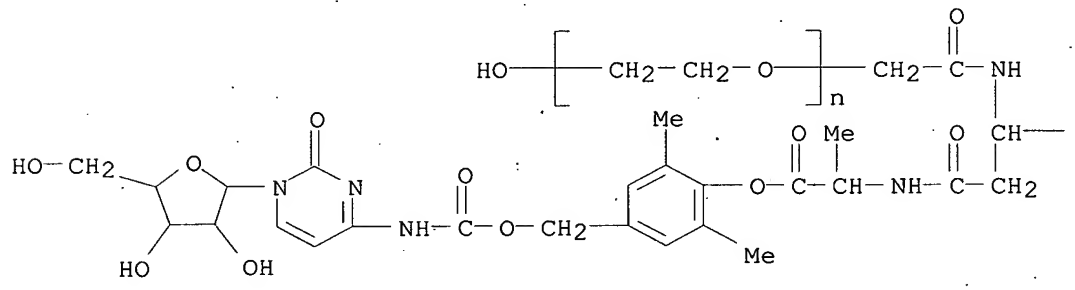
AB Terminally-branched polymeric prodrug platforms capable of high degrees of loading are disclosed. In preferred aspects of the invention, the prodrug platform releases multiple parent compds. after each branch holding the active agent undergoes a benzyl elimination reaction. Methods of preparing the prodrugs and using the same in the treatment of mammals are also disclosed. For example, a polyethylene glycol-cytosine arabinoside (PEG-Ara-C) conjugate was prepared The PEG-Ara-C conjugate demonstrated in tumor-bearing mice about equivalent antitumor activity with native Ara-C at only 20% of the active parent compound's dose. The IC50 for the PEG-Ara-C conjugate and the native Ara-C was 448 and 10 nM, resp., as determined in vitro using the P388/O (murine lymphoid neoplasm) cell line.

IT 452369-80-1P
RL: AMX (Analytical matrix); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)

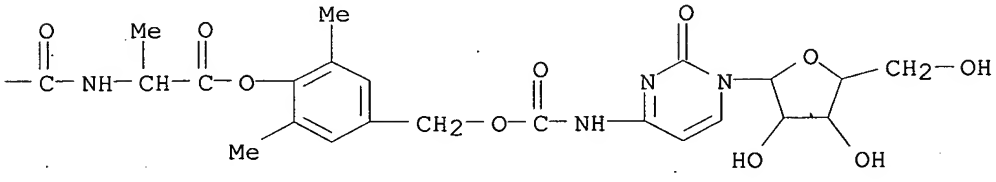
RN 452369-80-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 1-monoether with N-(hydroxyacetyl)-L-aspartoylbis[L-alanine] bis[4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



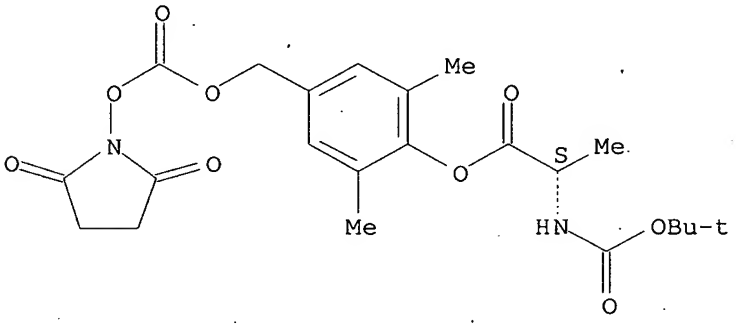
IT 452369-76-5P 452369-77-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)

RN 452369-76-5 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

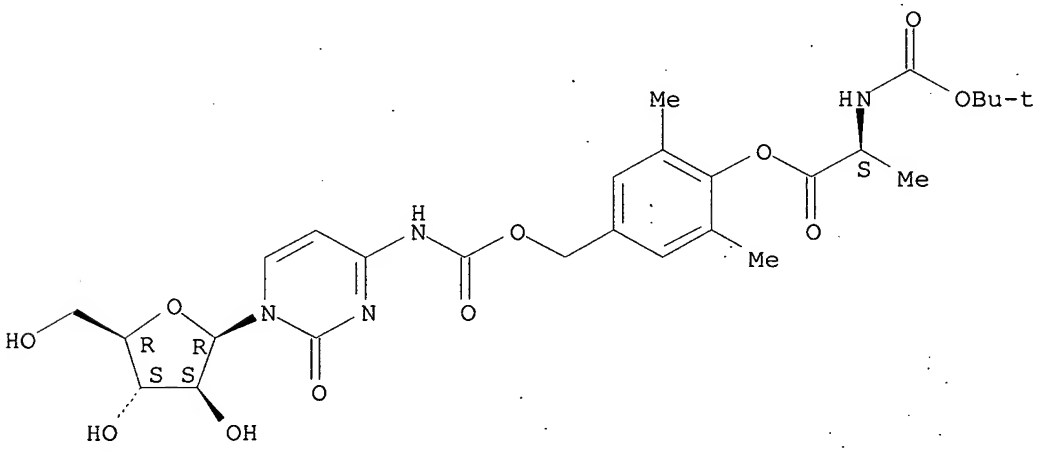
Absolute stereochemistry.



RN 452369-77-6 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:130614 HCAPLUS

DOCUMENT NUMBER: 137:341957

TITLE: Anticancer drug delivery systems: multi-loaded N4-acyl poly(ethylene glycol) prodrugs of ara-C. II. Efficacy in ascites and solid tumors

AUTHOR(S): Choe, Yun H.; Conover, Charles D.; Wu, Dechun; Royzen, Maksim; Gervacio, Yoany; Borowski, Virna; Mehlig,

Mary; Greenwald, Richard B.
CORPORATE SOURCE: Enzon, Inc., Piscataway, NJ, 08854-3969, USA
SOURCE: Journal of Controlled Release (2002), 79(1-3), 55-70
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

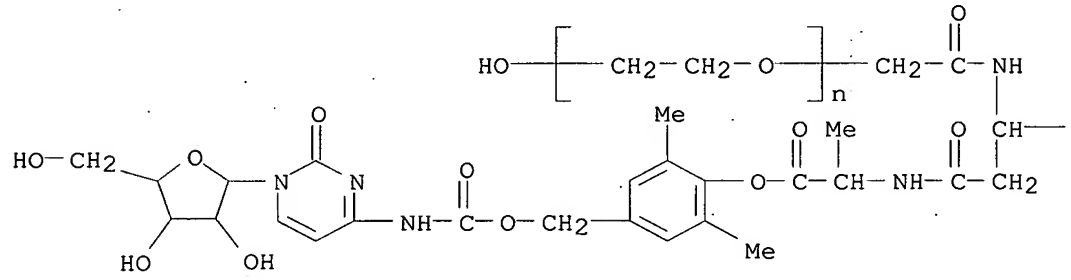
AB The synthesis of branched PEG (40,000) acids has been achieved using aspartic acid (Asp) and AspAsp dendrons. Complete conjugation of these dendritic acids with cytosine arabinoside (ara-C) was achieved by the use of spacers that allowed a greater separation of the branches to accommodate several large ara-C mols. in proximity to each other. The tetrameric and octameric PEG-ara-C amide prodrugs were much more effective in the treatment of solid and ascites tumors compared to the native drug. The greater loading of the PEG backbone appears to have achieved a min. threshold concentration for the therapeutic delivery of ara-C.

IT 452369-80-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and efficacy in ascites and solid tumors of multi-loaded N4-acyl polyethylene glycol prodrugs of ara-C)

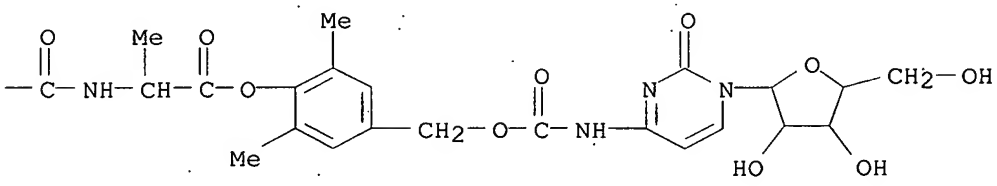
RN 452369-80-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 1-monoether with N-(hydroxyacetyl)-L-aspartoylbis[L-alanine] bis[4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



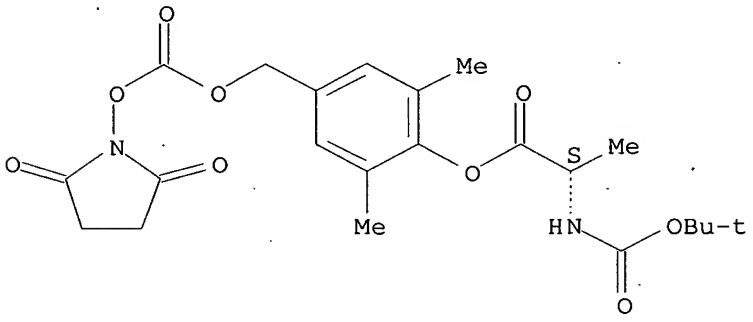
IT 452369-76-5P 452369-77-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and efficacy in ascites and solid tumors of multi-loaded N4-acyl polyethylene glycol prodrugs of ara-C)

RN 452369-76-5 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

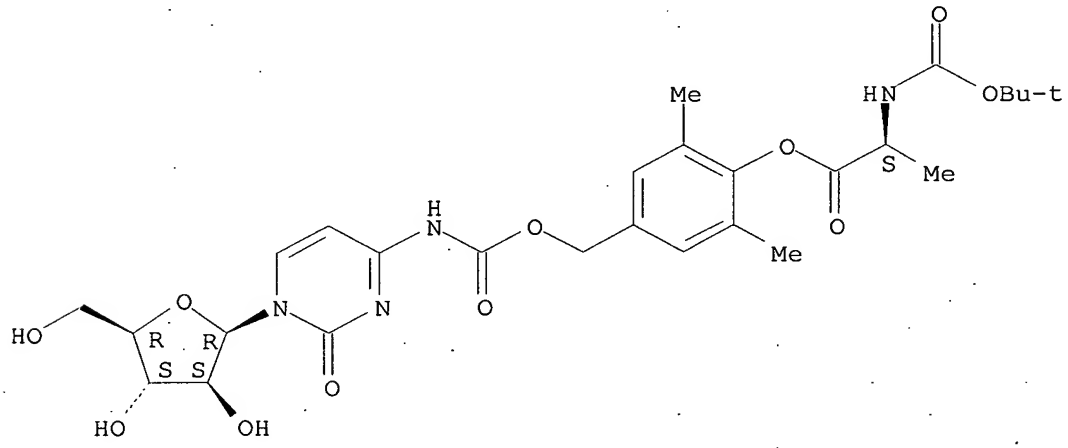
Absolute stereochemistry.



RN 452369-77-6 HCAPLUS

CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2004:299904 USPATFULL

TITLE: Polymeric oligonucleotide prodrugs

INVENTOR(S): Zhao, Hong, Edison, NJ, UNITED STATES
Greenwald, Richard B., Somerset, NJ, UNITED STATES

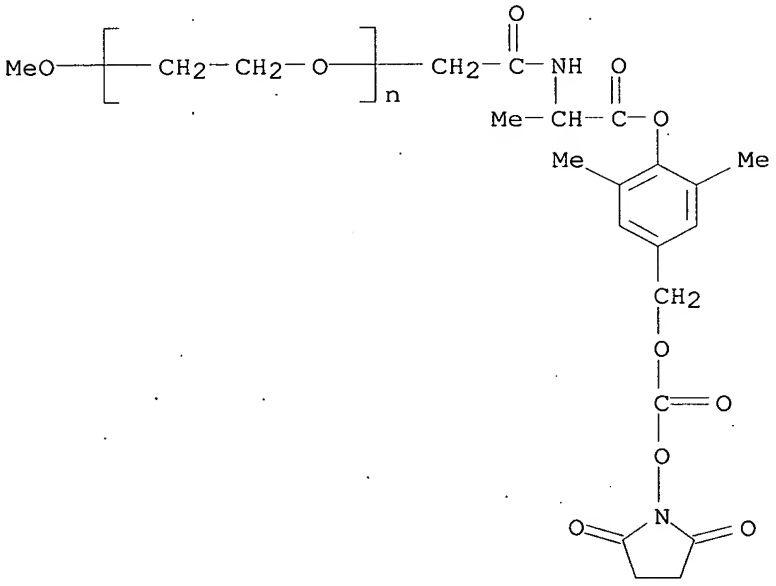
	NUMBER	KIND	DATE

PATENT INFORMATION:	US 2004235773	A1	20041125
APPLICATION INFO.:	US 2004-822205	A1	20040409 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-462070P	20030413 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MUSERLIAN, LUCAS & MERCANTI, LLP, 15th Floor, 475 Park Avenue South, New York, NY, 10016
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 1642
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polymer conjugates containing nucleotides and/or oligonucleotides are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 780810-34-6
(preparation of polyethylene glycol oligodeoxyribonucleotide conjugates as antitumor prodrugs)
RN 780810-34-6 USPATFULL
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1S)-2-[4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenoxy]-1-methyl-2-oxoethyl]amino]-2-oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2002:323093 USPATFULL
TITLE: Terminally-branched polymeric linkers and polymeric conjugates containing the same
INVENTOR(S): Choe, Yun Hwang, Green Brook, NJ, UNITED STATES

T.S. Heard Ph.D.

Greenwald, Richard B., Somerset, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183259	A1	20021205
APPLICATION INFO.:	US 2002-78730	A1	20020219 (10)

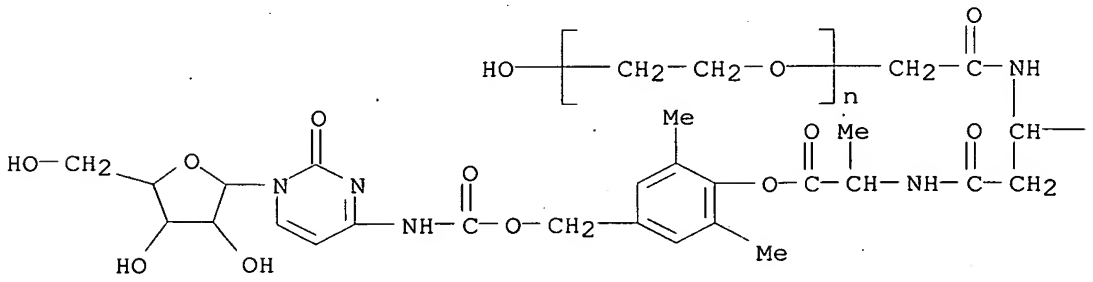
	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-270009P	20010220 (60)

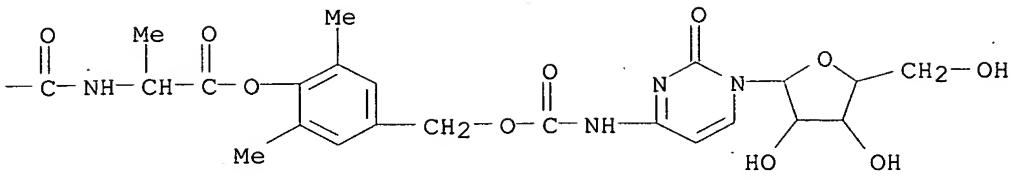
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael N. Mercanti, ROBERTS & MERCANTI, L.L.P., Suite 203, 105 Lock Street, Newark, NJ, 07103
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1429
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Terminally-branched polymeric prodrug platforms capable of high degrees of loading are disclosed. In preferred aspects of the invention, the prodrug platform releases multiple parent compounds after each branch holding the active agent undergoes a benzyl elimination reaction. Methods of preparing the prodrugs and using the same in the treatment of mammals are also disclosed. In one preferred aspect, polymeric conjugates such as ##STR1##

are provided.

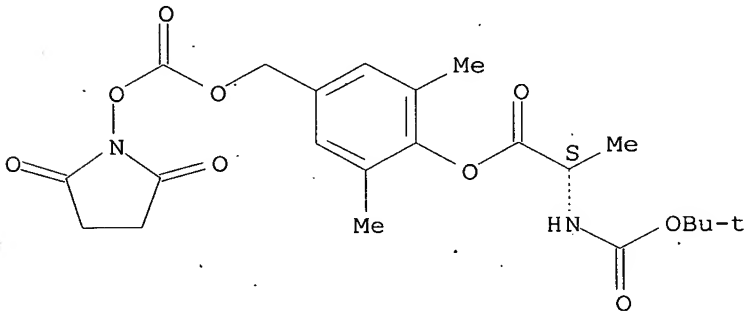
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 452369-80-1P
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)
RN 452369-80-1 USPATFULL
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 1-monoether with N-(hydroxyacetyl)-L-aspartoylbis[L-alanine] bis[4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl] ester (9CI) (CA INDEX NAME)





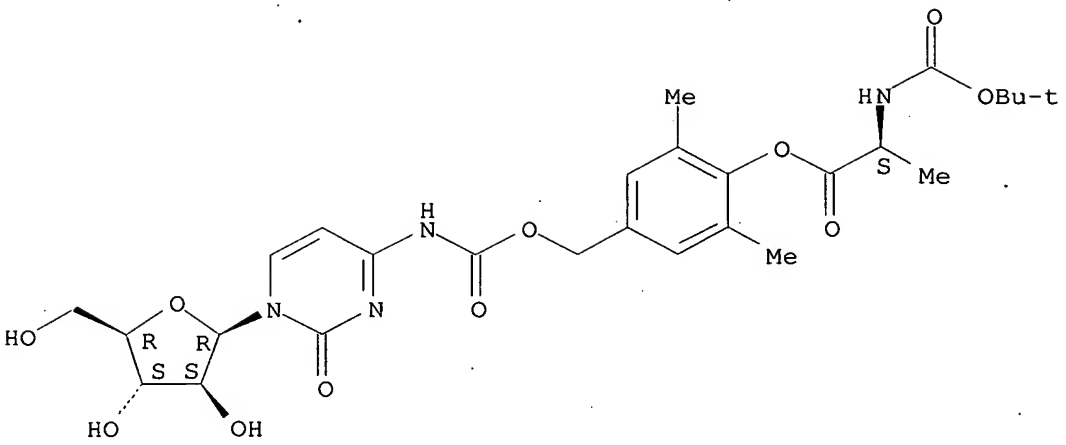
IT 452369-76-5P 452369-77-6P
(preparation of terminally-branched polymeric linkers and polymeric conjugates as prodrugs)
RN 452369-76-5 USPATFULL
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 452369-77-6 USPATFULL
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[[[[(1-β-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]carbonyl]oxy]methyl]-2,6-dimethylphenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.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